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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/945,731	os, Elaissari, Mabilat, Pichot, Rodrigue And Santo
Examiner	**Group Art Unit**
William Sandals	1636

X Responsive to communication(s) filed on Nov 10, 1997

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

X Claim(s) 1-20 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

Claim(s) _____ is/are allowed.

X Claim(s) 1-20 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

X See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

X Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

X All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____

X received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

Interview Summary, PTO-413

X Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Drawings

1. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

2. The use of the trademarks MILLEX, MILLI Q, THERMOMIXER, VIDAS, ESTAPOR and TRITON have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3, 10, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. The use of the language "according to a step" as a preamble for each of the steps in the methods of claims 1, 3 and 10, make the meaning of the method step difficult to understand and ambiguous, and as a result, the claims are indefinite. Deleting the language would make the meaning of the claims understandable without ambiguity.

6. In claim 10, lines 3-5, the language "the adsorption reagent is brought into contact with the nucleic material consisting of a probe or a primer in order to obtain a hybridization reagent" is unclear. It would appear that the probe or the primer has an antecedent basis which refers to the nucleic material, but this is not a certainty, and it might also refer to the adsorption reagent. Deleting "consisting of" and inserting --wherein the nucleic material consists of-- before "a probe" would make the antecedent basis of the probe and primer clear.

7. Claim 10 recites the limitation "(b')" in line 6. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 10 recites the limitation "hybridization reagent" in lines 8 and 9. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 15 recites the limitation "water-soluble cross-linking agent" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 16 recites the limitation "polymerization initiator" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itoh et al. (A3), Kausch et al. (B1), Kawaguchi et al. (B2) and Hoffman et al. (B3).

The claims are drawn to a process for the isolation of nucleic material in an aqueous phase by adsorption of the nucleic material on a solid acrylamide polymer which is made from a first monomer and a second monomer which is a copolymer which has been functionalized to adsorb the nucleic material at either a pH of 7 or less, an ionic strength buffer of less than 10^{-2} M, or a temperature less than the LCST of the polymer. After the adsorption step there is step to desorb the nucleic material by increasing the ionic strength of the buffer to greater than 10^{-2}, where the pH may be increased to greater than 7, or the temperature may be increased to be greater than the LCST of the polymer. The discontinuous phase (the solid acrylamide polymer) may be separated from the aqueous phase, and the separation may be done by filtration, centrifugation, sedimentation, precipitation or the application of a magnetic field. The solid acrylamide polymer

may be coated onto a non-adsorbing core which may be polystyrene, or may comprise a magnetic compound. The copolymer may comprise a nucleic acid fragment which may be a primer or probe, which may hybridize, under suitable conditions, to the nucleic material. Various acrylamide monomers for making the polyacryalmide are claimed, and as well, various cross-linking agents are claimed.

Itoh et al. taught (see especially pages 16, 18, 21, 24, 27, 44-45, 47-50 and claim 13) a process for the isolation of nucleic material in an aqueous phase by adsorption of the nucleic material on a solid acrylamide polymer which is made from a first monomer and a second monomer which is a copolymer which has been functionalized to adsorb the nucleic material at either a pH of 7 or less, or a temperature less than the LCST of the polymer. After the adsorption step there is step to desorb the nucleic material by increasing the pH, or the temperature may be increased to be greater than the LCST of the polymer. The copolymer may comprise a nucleic acid fragment which may be a primer or probe, which may hybridize, under suitable conditions, to the nucleic material. Various acrylamide monomers for making the polyacryalmide are claimed, and as well, various cross-linking agents are claimed. Itoh et al. taught the use of the method with the copolymer being an affinity ligand.

While Itoh et al. did not specifically teach the use of a low ionic strength binding buffer nor the increased ionic strength of an eluting buffer, one of ordinary skill in the art would know that the use of an affinity matrix would require the use of elements such as a low ionic strength binding buffer and an increased ionic strength buffer to elute the bound nucleic material.

Itoh et al. did not teach the discontinuous phase (the solid acrylamide polymer) may be separated from the aqueous phase, and the separation may be done by filtration, centrifugation, sedimentation, precipitation or the application of a magnetic field, nor where the solid acrylamide polymer may be coated onto a non-adsorbing core which may be polystyrene, or may comprise a magnetic compound.

Hoffman et al. taught (see especially the Summary of the invention and column 9, line 15 bridging to column 10, line 51) the use of an acrylamide polymer such as NIPAM, which was copolymerized with monomers which bound nucleic acids and proteins where the moiety of interest was adsorbed at an temperature below the LCST of the polymer and then desorbed at a temperature above the LCST. Hoffman et al. also taught the adsorption of a desired moiety onto the polymer with a low ionic strength buffer and the desorption of the desired moiety with a high ionic strength buffer.

Kawaguchi et al. taught (see especially columns 3-8) an acrylamide polymer coated onto beads which were bound to DNA which were used to bind proteins at a low ionic strength and elute the proteins at a high ionic strength, where the beads did not non-specifically adsorb proteins. The beads were isolated by centrifugation or filtration.

Kausch et al. taught (see especially the abstract and columns 3-10) an acrylamide polymer coated onto beads which comprised a magnetic compound. The acrylamide polymer coated beads were used to reversibly bind DNA using probes. The binding reaction took place in low ionic strength buffer and the release was effected with high ionic strength buffer. The magnetic

compound in the acrylamide coated beads allowed the isolation of the bound material by a magnetic field.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Itoh et al., Hoffman et al., Kawaguchi et al. and Kausch et al. to produce the instant invention because Itoh et al., Hoffman et al., Kawaguchi et al. and Kausch et al. were all using acrylamide polymers with a copolymer which would adsorb and desorb nucleic acids and proteins. Itoh et al. taught the use of the acrylamide polymer in bead form, and coated onto solid supports. Hoffman et al. taught the adsorption of nucleic acid in a low ionic strength buffer and the desorption of the nucleic acid in a high ionic strength buffer. Kawaguchi et al. and Kausch et al. taught the coating of polyacrylamide onto solid bead supports, and Kausch et al. taught the polyacrylamide coated beads which comprised a magnetic compound to facilitate the isolation of the bead with the bound DNA in a magnetic field.

One of ordinary skill in the art would have been motivated at the time of the instant invention to combine the teachings of Itoh et al., Hoffman et al., Kawaguchi et al. and Kausch et al. to produce the instant invention because Itoh et al., Hoffman et al., Kawaguchi et al. and Kausch et al. taught the desirable use of acrylamide polymers with a copolymer which would adsorb and desorb nucleic acids and proteins. Itoh et al. taught the use of the acrylamide polymer in bead form, and coated onto solid supports. Hoffman et al. taught the desirable method of adsorption onto an acrylamide solid support of nucleic acid in a low ionic strength buffer and the desorption of the nucleic acid in a high ionic strength buffer. Kawaguchi et al. and Kausch et al.

taught the coating of polyacrylamide onto solid bead supports, and Kausch et al. taught the polyacrylamide coated beads which comprised a magnetic compound to facilitate the isolation of the bead with the bound DNA in a magnetic field. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Itoh et al., Hoffman et al., Kawaguchi et al. and Kausch et al.

Conclusion

13. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.
Examiner
September 15, 1998

George C. Elliott, Ph.D.
Supervisory Patent Examiner
Technology Center 1600